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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/575,831 | 02/05/2007 | Ying C.Q. Zang | 050989.0203.01USPC | 2074 |

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| EXAMINER | |
|---|---|
| EWOLDT, GERALD R | |

| ART UNIT | PAPER NUMBER |
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| 1644 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/575,831 | ZANG, YING C.Q. | |
| | Examiner | Art Unit | |
| | G. R. Ewoldt, Ph.D. | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *8-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/14/06* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/22/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence Notice to Comply*.

**DETAILED ACTION**

1. Applicant's election with traverse of Group I in the paper filed 3/26/09 is acknowledged.

Applicant argues that the subject matter of the claims is naught taught nor suggested by the cited references.

As set forth below in Sections 7 and 9, the claimed method is neither novel nor does it comprise an inventive step. Accordingly, a lack of unity of invention has been established and restriction is proper.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 8-14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected inventions.

Claims 1-7 are under examination.

3. The Title and Abstract are objected to because they do not adequately describe the claimed invention. Applicant is advised that a Title commensurate in scope with the invention of the instant claims, e.g., "A method of making an autologous $CD8^+$ T cell vaccine for treating multiple sclerosis", is required. An Abstract disclosing said method is also required. See MPEP 608.01(b).

4. The drawings are objected to for the following reasons:
A) The text labeling the axes in Figure 3 is illegible.
B) The symbols in the graphs of Figure 6A are illegible.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional

replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action.

The objection to the drawings will not be held in abeyance.

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Specifically, the Sequence Listing fails to disclose all of the priority documents at line <150>.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-3, 5, and 6 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Jurewicz et al. (1998) as evidenced by U.S. Patent No. 6,806,258.

Jurewicz et al. teaches the claimed method of making a $CD8^+$ T cell composition comprising:

A) providing PBMCs,

B) reducing the number of $CD4^+$ T cells (by enriching for $CD8^+$ T cells),

C) adding the MS-associated antigen comprising the MBP peptide of SEQ ID NO:3, APCs, and IL-2, and

D) repeating the process. (see particularly CD8 T cell lines, bridging pages 3056 and 3057).

Note that the '258 patent is cited merely to show that IL-2 can be considered to be a T cell mitogen (see particularly column 1, last paragraph),

The reference teaching anticipates the claimed invention.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 03/024393 (IDS) in view of Huseby et al. (2001, IDS).

WO 03/024393 teaches the claimed method of making a T cell vaccine including the use of MS-associated antigens including MBP and MBP fragments 83-99 and 151-170 and the inclusion of a mitogen including conA (see particularly page 2, 3rd full paragraph - page 3, 1st paragraph).

The reference teaching differs from the claimed invention only in that it does not teach reducing the population of $CD4^+$ T cells in the vaccine.

Huseby et al. teaches that MBP-specific $CD8^+$ T cells induce severe CNS autoimmunity in wild-type mice (see particularly, page 670, *MBP-specific $CD8^+$ T Cells Induce CNS Autoimmunity*). The reference further teaches the $CD8^+$ T cells are direct effectors of disease because they induce disease in scid mice (see particularly, Figure 2). The reference further teaches that $CD25^+CD4^+$ T cells "perform a regulatory function in inhibiting autoimmunity" (see particularly, page 673, column 1). Finally, the reference teaches that the disease of the MBP-CTL-mediated model resembles the Pattern IV disease of Lucchinetti et al. (2000) seen in some PPMS patients (see particularly page 674, column 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the T cell vaccine of WO 03/024393 enriched for $CD8^+$ T cells, i.e., with a reduced population of $CD4^+$ T cells, given the teachings of Huseby et al. First, Huseby et al. teaches that $CD8^+$ T cells can be direct effectors of CNS autoimmunity (and would thus, comprise an obvious vaccine target). Additionally,

the reference teaches that the MBP-CTL-mediated model disease resembles the disease seen in some PPMS patients. Accordingly, the ordinarily skilled artisan would be motivated to produce a T cell vaccine enriched in $CD8^+$ T cells if only specifically for the treatment of Pattern IV PPMS. Additionally, the ordinarily skilled artisan would be motivated to reduce the number of $CD4^+$ T cells in the vaccine because of the regulatory function of $CD25^+CD4^+$ T cells. Given said regulatory function the ordinarily skilled artisan would not want to produce a vaccine targeting those regulatory T cells.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571)272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on (571) 272-0878.

12. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

/G.R. Ewoldt/
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